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Breast Cancer

The impact of the COVID-19 pandemic on surgical management of breast cancer: global trends and future perspectives.

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Key Words. Breast cancer surgery • COVID-19 • triage • surgical priorities • alternatives to surgery

Abstract

Introduction. The rapid spread of COVID-19 across the globe is forcing surgical oncologists to change their daily practice. We sought to evaluate how breast surgeons are adapting their surgical activity to limit viral spread and spare hospital resources.

Methods. A panel of 12 breast surgeons from the most affected regions of the world convened a virtual meeting the 7th of April 2020 to discuss the changes in their local surgical practice during the COVID-19 pandemic. Similarly, a web-based poll based was created to evaluate changes in surgical practice among breast surgeons from several countries.

Results. The virtual meeting showed that distinct countries and regions were experiencing different phases of the pandemic. Surgical priority was given to patients with aggressive disease not candidate for primary systemic therapy, those with progressive disease under neoadjuvant systemic therapy, and post-neoadjuvant patients. One hundred breast surgeons filled out the poll. The trend showed reductions in operating room schedules, indications for surgery, and consultations, with an increasingly restrictive approach to elective surgery with worsening of the pandemic.

Conclusion. The COVID-19 emergency should not compromise treatment of a potentially lethal disease such as breast cancer. Our results reveal that physicians are instinctively reluctant to abandon conventional standards of care when possible. However, as the situation deteriorates, alternative strategies of de-escalation are being adopted. ***The Oncologist*** 2020;9999:• •

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Implications for Practice: Our study aims to characterize how the COVID-19 pandemic is affecting breast cancer surgery and which strategies are being adopted to cope with the situation.

Background

The COVID-19 pandemic is affecting health resources on a global scale with a significant impact on oncological management[1]. Clinicians must balance standard cancer therapies with measures designed to limit the spread of COVID-19. At the same time, healthcare workers face many challenges including shortage of resources (e.g. personal protective equipment), excessive working hours and psychological distress[2-4].

Breast cancer (BC) is a common disease affecting 1 in 8 western women and is potentially lethal[5]. For the majority of early stage patients, surgery remains the primary treatment, but delays from diagnosis to start of treatment of less than 90 days does not appear to adversely impact prognosis[6]. This rule, however, does not apply to all clinical scenarios and patients who need surgery more urgently should be identified through appropriate and effective triage[7]. Decisions on treatment must take into account the individual risk of exposure and infection and balance it with the potential risk of a worse oncological outcome if the appropriate treatment is not commenced in a timely fashion.

According to World Health Organization (WHO), social distancing, quarantine (for asymptomatic COVID-19-positive patients, people who came in contact with COVID-19 positive patients and people coming from areas with high number of COVID-19 cases) and wearing face masks when in proximity to others are the most effective measures to control the spread of COVID-19. These measures can help to slow down the rate of new infections, allowing healthcare systems to cope with clinical demand and allocate sufficient resources in the quest for an effective therapy and continuing ongoing research[8,9].

However, the combination of social distancing and reduced resources may clash with the surgical management of breast cancer patients.

This study aims to examine the changes in the surgical management of breast cancer patients during the different phases of the COVID-19 pandemic. . Results of this study will provide better understanding of how healthcare systems rapidly adapt to a new crisis and highlight key elements for planning the recovery phase.

Materials and Methods

G.Re.T.A. (Group for Reconstructive and Therapeutic Advancements), is an international organization founded in 2017 that aims to bring together breast cancer specialists in order to advance multidisciplinary educational and research activity[10]. The organization convened a virtual meeting entitled "the surgical management of breast cancer during the COVID-19 emergency". A web-based poll designed to explore the different approaches and responses during the COVID-19 pandemic was launched 3 days prior to the scheduled meeting.

Virtual meeting

A panel of 12 dedicated breast surgeons from 9 countries across three continents were invited to participate in a virtual meeting held on the 7th of April at 4.00 PM GMT+1. The panel included breast surgeons from those areas most affected at the time by COVID-19 (Iran, Italy, Spain, UK, and USA) together with other specialists from China, Denmark, Portugal, Sweden, and Switzerland.

All panel members were invited as spokespersons for their respective multidisciplinary team.

In addition, an experienced medical oncologist (CC) was invited to contribute and supervise the multidisciplinary discussion. Panelists discussed the following topics in accordance with corresponding national and local/institutional guidelines:

a) Pandemic phase according to American College of Surgeons[7]

b) Triage and management of new breast clinic referrals and breast cancer diagnoses

c) Surgical priorities

d) Alternatives to surgery

e) Management of admitted patients (including operating room)

f) Management/Modalities of consultations

The virtual meeting was advertised through the G.Re.T.A. institutional website and on social media. Ninety participants joined the meeting.

Web-based poll

An anonymous web-based poll was set up on the 4th of April 2020, and all the panelists and the participants to the virtual meeting were invited to participate. The poll was also circulated through G.Re.T.A. social media in order to reach the largest scheduled number of participants. The poll was based on the "American College of Surgeons: COVID-19 Elective Case Triage Guidelines for Surgical Care of Breast Cancer" issued on the 24th of March 2020 by the ACS and available on-line[7] (ACS weblink) (Supplemental material 1).

ICU Intensive Care Unit

The questionnaire included eight items (Supplemental material 2):

- Geographical area
- Position of participant
- Pandemic phase according to the aforementioned guidelines
- Priorities in breast cancer surgical management (cases to be done as soon as possible)
- Cases that can be deferred
- Alternative treatment approaches to be considered
- Modalities of consultations/long term follow-up

- Operating room schedule

Due to the rapid evolution of the pandemic, a pre-specified number of total participants was fixed at 100. The poll closed on April 14th after reaching the pre-specified goal.

Data Analysis

Replies were grouped according to geographical area experiencing a similar phase of the pandemic . Replies to topic d-e-f-g-h are listed according to progressive restrictions. Due to the reduced sample size and in order to perform statistical analysis, we grouped variables to become bivariate (i.e. standard vs. restricted modalities) (Supplemental material 3). Response rates were compared among groups using Fisher's exact test. P-values < 0.05 were considered statistically significant. Statistical analysis was performed using SPSS (Version 25.0. Armonk, NY: IBM Corp).

Results

Virtual meeting

On of the meeting day, different countries and regions were in different phases of the pandemic[11], and therefore participants were in different ACS phases. This was true also within the same country and within large cities.

Differences were observed in the surgical management of BC among panelists from different countries, and from different institutions within the same country (private vs. public hospitals, academic or tertiary care) and are summarized in Table 1. In some countries multiple guidelines and consensus statements issued from different scientific societies and institutions were available[7,12-14], whereas in other countries equally affected, no specific breast surgery related guidelines had been released by entitled entities.

The lockdown starting date varied from 23rd January 2020 in China (where it was already concluded at the time of the meeting) to 29th March (Spain). Notably, this measure was not applied in Sweden, where social distancing was voluntary.

BC screening programs were halted in most countries, except for Sweden and Denmark. Most of the countries in phase 2-3 had implemented a triage system (the day before or the day of admission), that took place at the hospital or via tele-consultation in advance of any face-to-face (FTF) encounter (UK/USA). Screening methods varied between and within countries, ranging from clinical history only, to temperature assessment with screening and SpO2 check and nasopharyngeal swabs with chest X-ray/CT-scan. Nasopharyngeal swabs with negative results were mandatory before surgery in Spain, Portugal, Switzerland and in Italy (with variations according to local institution policy). In other countries, polymerase chain reaction testing on swabs were indicated only for symptomatic patients (Italy, UK, Sweden, Denmark). Allocation of single rooms was routinely adopted in China and the use of masks by patients was strongly recommended in all countries.

Same day discharge policy wherever possible was preferred although not mandatory (Italy, Spain, UK, Sweden, Denmark and in the USA).

Surgical prioritization varied between countries and according to the phase of the pandemic. China had resumed standard clinical practice, whereas Italy, the USA and UK were prioritizing urgent cancer cases in anticipation of the need for intensive care unit (ICU) facilities. Priorities for surgery included patients with progressive disease while on neoadjuvant chemotherapy (NAC), post-NAC patients, patients with small triple negative (TN) and human epidermal growth factor (HER2) positive, or T2 N0 hormone receptor (HR) positive /HER2- not deemed eligible for neoadjuvant treatment cases (Italy). In Italy/Spain/UK, ductal carcinoma in situ (DCIS) patients were not considered a priority and could be deferred (Italy >8 weeks) depending on ventilator availability. In the USA/UK, receptor status testing was recommended for all cases of DCIS and endocrine therapy was recommended for hormone HR+ DCIS[12,13]. There was consensus across countries that primary systemic treatment was an acceptable alternative strategy to defer surgical excision and should be based on national/international guidelines. In both the UK/USA, it was considered acceptable to defer surgery by commencing primary endocrine treatment in patients with HR+/HER2-, node negative tumors. Due to the broadening of indications for preoperative therapy, genomic (or Ki-67/grade) testing of core biopsy material was discretionary for some higher risk tumors.

The majority of panelists deferred immediate breast reconstruction (IBR), especially more complex autologous flap-based procedures, yet most considered two stage implant-based IBR a safe and manageable option.

Web-based poll

A total of 100 breast surgeons completed the poll, with the majority (90%) being fully accredited surgeons and only 10% trainees. Two-thirds of respondents (63%) worked in a Phase 1 setting with relatively few COVID-19 patients and availability of ICU beds. Just over one-third were based in the most severely affected European areas (Italy, Spain, France and UK), with just 19% from South America, 8% from Iran and the remaining 35% from other countries.

The poll revealed a general contraction of breast surgical capacity across the world as seen in Figure 1.

As the pandemic worsened with increasing demand for ICU and ventilator facilities, there was a gradual shift from elective to emergency surgery only (Figure 2).

Similarly, the total number of FTF consultations fell across all countries surveyed (Figure 3) with suspension of routine follow-up visits and acceptance of urgent referrals only in more than three-quarters of units in phase 1 (84%) and all those (100%) in phase 3.

Just over half of respondents (52%) prioritized surgery following NAC, for T2 N1 HR+/HER2- cancers, for discordant biopsies likely to be malignant, and for excision of malignant recurrence.

There was a statistically significant association between the level of surgical restriction and the pandemic phase ($p = 0.001$), as shown in Figure 4.

Overall, the great majority (88%) of surgeons deferred benign cases, bilateral procedures and autologous reconstructive surgery (Figure 5). With progression of the pandemic from phase 1 to 3, surgeons also deferred in situ HR+ disease as well as re-excision cases.

Almost half (48%) of respondents offered primary systemic treatments as an alternative to surgery for the following categories of tumor:

- T1N0 HR+/HER2- : endocrine therapy
- TN and HER2+ tumors: neo-adjuvant chemotherapy +/- single/dual anti HER2 agents
- some T2 or N1 HR+/HER2- cancers: endocrine therapy
- N1 cancer irrespective of subtype: neo-adjuvant chemotherapy

This approach was more likely to be adopted by participants with increasing severity of the COVID-19 pandemic (40% in phase 1, 62% in phase 2 and 67% in phase 3). Fourteen and 8% of participants in phases 1 and 2, respectively, did not change their clinical decision-making process in regard to neo-adjuvant treatments (Figure 6).

Discussion

Resources and surgical management

Changes in the management of newly diagnosed breast cancer in response to COVID-19 varied according to geographic area and pandemic phase, but also between different institutions within a particular country. The unprecedented speed and scale of the outbreak precluded the establishment of any formal guidelines based on international consensus.

Our survey confirms a global reduction in the volume of elective breast surgery that may be attributable to either a shortage of facilities and limited surgical capacity during the crisis or possibly to social distancing imposed by health authorities with resultant limited access to healthcare in general.

In principle, patients are prioritized for surgery based on completion of neo-adjuvant chemotherapy, small (T1/N0) TNBC or HER2 subtypes and T2 or N1 HR+/HER2- tumors. In the event of a shortage of ventilatory and operating room capacity, a crucial question is how long surgical management can be deferred without impairment of clinical outcomes. In a joint analysis of the Surveillance, Epidemiology, and End Results (SEER)-Medicare-linked database and the National Cancer Database (NCDB), delays of more than 90 days from diagnosis to treatment have been shown to be associated with reduction in overall survival rates of 3.1-4.6%[6]. By implication, it might therefore be considered appropriate to schedule surgery for within 90 days if no other treatment is commenced as primary therapy.

However, when breast surgery is performed its impact on the healthcare system is relatively modest; there are relatively short operating times and limited need for intensive care facilities with much surgery being performed as a day case procedure with few complications. The re-admission rate for complications following breast surgery as estimated by the American College of Surgeons-National Surgical Quality Improvement Program (ACS-NSQIP) database is approximately 4% within 30 days[15]. The post-surgical ICU admission rate after breast surgery is estimated 1.8% and not comparable to major surgery[16]. Few complications following breast surgery mean also less patients coming back to hospital for post-surgical consultation or secondary procedures, and consequently less urban mobility both of patients and care-givers.

Our survey confirms that theatre lists can be managed with relatively few resources and breast surgeons tend to use any residual capacity to operate (even in phase 2).

Special considerations apply to immediate breast reconstruction (IBR) and these are very much dependent on local circumstances and operative capacity. Increased complication rates are associated with IBR (14.2% for implant-based and 15.4% for autologous compared with 4.2% without IBR) and this has prompted some countries to limit all forms of IBR and in particular stop autologous tissue-based reconstruction[17]. For younger patients wishing to preserve the skin envelope, a "babysitter implant" or a formal epipectoral approach may be an option but might lead to additional post-operative visits and potential re-admission to hospital. Most of the participants deferred bilateral procedures (such as most of stage II of tissue-expander/implant reconstructions), or autologous reconstructions. According to the poll and during phase progression more restrictive indications prevented also re-excisions and excision biopsy of uncertain lesions.

Alternatives to surgery

With the unprecedented circumstances of the COVID-19 pandemic in which there are potential shortages of ventilator equipment and ICU personnel, professional bodies have recommended alternative therapeutic options as a short-term imperative. These are not necessarily based on published data but reliant on "educated assumptions and expert opinion"[18].

The panel relayed information on national and institutional recommendations for COVID-19 protocols with several links available to association websites[7,12,13,19]. The ACS triage, for instance is recommending 6-12 months of primary endocrine treatment in luminal A or Oncotype DX <25% tumors[7]. However, before the current pandemic the NCCN guidelines supported use of primary endocrine therapy mainly in patients with co-morbidities and low risk ER+ invasive breast cancer[20]. Historically, this treatment has been used for elderly patients with co-morbidities who were considered unfit for surgery[21-23]. Concerns exist regarding pre-operative endocrine therapy for pre-menopausal women or for those with longer life expectancy[24]. The ideal duration of pre-operative endocrine treatment is unclear, but usually it should be given for at least 6 months and in case of lack of response, surgery should be carried out[25-27]. In some countries, primary endocrine therapy is also advised for HR+ DCIS, and hence all core biopsies should be tested for HR[12,13]. These approaches are in line with trials investigating non-operative management of low risk DCIS where primary endocrine therapy may be an option in the observation arm[28-30]. Nonetheless, observation alone can be considered for smaller low-risk DCIS irrespective of HR status and

pending operative availability[12]. Outcomes for DCIS managed without loco-regional intervention were investigated using the SEER database and low rates of progression to invasive disease was demonstrated. However, results may have been confounded by concurrent use of systemic endocrine treatment in some patients[31].

The poll revealed that a sizable proportion of participants considered primary chemotherapy to be routine for many patients with specific subtypes of breast cancer, namely TNBC and HER2+. This practice could be extended to all N1 patients irrespective of HR status, and to some larger T2 HR+,/HER2- cancers. Indeed, a trend for broadening indications for primary systemic therapy was evident with increasing gravity of the pandemic and pressure upon emergency services.

Some experts according to national societies are suggesting to use genomic testing pre-operatively to identify HR+/HER2- cancers which may be chemo-sensitive in order to defer surgery and give NAC irrespective of tumor stage[32].

Some experts, conversely, report a particular concern about the risk of COVID-19 infection, due to immunosuppression, for patients undergoing chemotherapy. This had led some countries to restrict, instead of expanding, the indications to neoadjuvant chemotherapy for patients with early stage disease[13].

Management of screening, outpatient workload and referrals

Universal suspension of breast cancer screening services has been reported from around the world. Depending on the duration of shutdown, there may or may not be any clinically meaningful impact on breast cancer mortality. It is also unclear whether during the recovery phase, rules of social distancing will impact on the number of women invited per each screening session.

Evidence for re-organization of FTF consultations has emerged from this poll and this applies to both newly diagnosed symptomatic breast cancers and post-operative cases. According to the amended guidelines of the “the COVID-19 Pandemic Breast Cancer Consortium”, in person visits should be converted to telemedicine, whenever possible, unless there is clinical urgency for FTF consultation [33]. The COVID-19 pandemic has allowed widespread conversion to telemedicine demonstrating its utility as an effective tool for social distancing in the clinical setting and for reducing outpatient workload without compromising optimal care. In the current crisis, telemedicine can be used to communicate both benign and malignant pathology results and to initiate endocrine treatment as primary or adjuvant therapy. Of course, reliable infrastructures should be available across the world, as well as trained staff, a validated workflow and safe management of individual data[34]. The quality of care in telemedicine should be comparable to in-person care, although physical examination is necessarily precluded. Nonetheless, the overall care process should not be compromised in any way that might threaten patient safety. Robust protocols must exist that permit discrimination between visits that can safely be performed in telemedicine and those mandating physical examination.

In some regions of the world affected by COVID-19 , local governments have opted for COVID-dedicated and COVID-free/ light hospitals, for treatment of specific conditions. For example, In the UK, USA and parts of Italy some dedicated cancer hospitals have continued to offer oncological care within standard timeframes and adhered to routine management protocols. A negative pharyngeal swab before access to these facilities was essential and patients were treated only if COVID-19 negative. In some institutions cancer surgery was deferred for COVID -19 positive patients pending resolution of symptoms and two subsequent negative swabs (COVID-free hospitals) while others reserved clinical and operating areas for treatment of COVID-19 positive patients.

Conclusions

Approximately 150,000 new cases of breast cancer are diagnosed every month worldwide. Once screening has been suspended and breast consultations reduced, a delays in diagnosis of small screen-detected and some symptomatic cancers might be expected. However any delays attributable to COVID-19 are unlikely to have any prognostic impact for these indolent slow growing tumours nor indeed for cases of ‘over-diagnosis’. This is why in the post pandemic phase criteria for prioritization will continue to be refined and aid in selecting those patients who are appropriate candidates for primary surgery.

The unexpected contingency of COVID-19 should not compromise the management of a potentially lethal disease like breast cancer. The results of this survey highlight a trend towards reduction of theatre lists and out-patient facilities that is escalating across emergency phases. Our survey shows that physicians individually can be reluctant to abandon standards, change surgical priorities or escape to alternative treatments until operating rooms are not available. However, more restrictions or alternative strategies are accepted as the situation worsens.

Access to cancer therapy should be managed in order to offer a level of care as close as possible to the standards. Now more than ever, multidisciplinary discussion regarding priority for treatments on a case-by-case basis is highly recommended. Communication between surgical oncologist and health-care authorities is largely awaited. Notwithstanding the importance of control measures, breast cancer surgery is not per se resource consuming and it should be performed even with minimal capacity.

In this context, surgeons and health systems in general are invited to be resilient. This means that: every strategy to get the same surgical outcomes should be pursued; the waiting times should be used to increase pre-habilitation; observation or use of alternative therapeutic strategies should be performed within randomized trials or under strict surveillance.

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References

1. The Lancet O. COVID-19: global consequences for oncology. Lancet Oncol. 2020;21(4):467.

2. Remuzzi A, Remuzzi G. COVID-19 and Italy: what next? Lancet. 2020;395(10231):1225-1228.

3. Mitchell R, Banks C, authoring working p. Emergency departments and the COVID-19 pandemic: making the most of limited resources. Emerg Med J. 2020.

4. Galea S, Merchant RM, Lurie N. The Mental Health Consequences of COVID-19 and Physical Distancing: The Need for Prevention and Early Intervention. JAMA Intern Med. 2020.

5. Sharma R. Breast cancer incidence, mortality and mortality-to-incidence ratio (MIR) are associated with human development, 1990-2016: evidence from Global Burden of Disease Study 2016. Breast Cancer. 2019;26(4):428-445.

6. Bleicher RJ, Ruth K, Sigurdson ER, et al. Time to Surgery and Breast Cancer Survival in the United States. JAMA Oncol. 2016;2(3):330-339.

7. American College of Surgeons. https://www.facs.org/covid-19/clinical-guidance/elective-case. Published 2020. Accessed 10/04/2020.

8. Koo JR, Cook AR, Park M, et al. Interventions to mitigate early spread of SARS-CoV-2 in Singapore: a modelling study. Lancet Infect Dis. 2020.

9. Lau H, Khosrawipour V, Kocbach P, et al. The positive impact of lockdown in Wuhan on containing the COVID-19 outbreak in China. J Travel Med. 2020.

10. Group for Reconstructive and Therapeutic Advancements. https://greta.maurizionava.it. Published 2020. Accessed 17/04/2020.

11. Johns Hopkins University of Medicine Coronavirus Resource Center. https://coronavirus.jhu.edu/map.html. Published 2020. Accessed 7/4/2020.

12. Society of Surgical Oncology. https://www.surgonc.org/wp-content/uploads/2020/03/-Breast-Resource-during-COVID-19-3.30.20.pdf. Published 2020. Accessed 10/04/2020.

13. Association of Breast Surgery. https://associationofbreastsurgery.org.uk/news/2020/-abs-statement-re-covid-19/. Published 2020. Accessed 10/04/2020.

14. Soran A, Gimbel M, Diego E. Breast Cancer Diagnosis, Treatment and Follow-Up During COVID-19 Pandemic. Eur J Breast Health. 2020;16(2):86-88.

15. Al-Hilli Z, Thomsen KM, Habermann EB, Jakub JW, Boughey JC. Reoperation for Complications after Lumpectomy and Mastectomy for Breast Cancer from the 2012 National Surgical Quality Improvement Program (ACS-NSQIP). Ann Surg Oncol. 2015;22 Suppl 3:S459-469.

16. Puxty K, McLoone P, Quasim T, Sloan B, Kinsella J, Morrison DS. Characteristics and Outcomes of Surgical Patients With Solid Cancers Admitted to the Intensive Care Unit. JAMA Surg. 2018;153(9):834-840.

17. O'Connell RL, Rattay T, Dave RV, et al. The impact of immediate breast reconstruction on the time to delivery of adjuvant therapy: the iBRA-2 study. Br J Cancer. 2019;120(9):883-895.

18. van de Haar J, Hoes, L.R., Coles, C.E. et al. Caring for patients with cancer in the COVID-19 era. Nat Med 2020.

19. Italian Society of Surgical Oncology. https://www.sicoweb.it/raccomandazioni-sico.pdf. Published 2020. Accessed 18/10/2020.

20. National Comprehensive Cancer Network: NCCN Clinical Practice Guidelines in Oncology BC. https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf. Published 2020. Accessed 10/04/2020.

21. Chia YH, Ellis MJ, Ma CX. Neoadjuvant endocrine therapy in primary breast cancer: indications and use as a research tool. Br J Cancer. 2010;103(6):759-764.

22. Bergman L, van Dongen JA, van Ooijen B, van Leeuwen FE. Should tamoxifen be a primary treatment choice for elderly breast cancer patients with locoregional disease? Breast Cancer Res Treat. 1995;34(1):77-83.

23. Hind D, Wyld L, Beverley CB, Reed MW. Surgery versus primary endocrine therapy for operable primary breast cancer in elderly women (70 years plus). Cochrane Database Syst Rev. 2006(1):CD004272.

24. Dowsett M, Ellis MJ, Dixon JM, et al. Evidence-based guidelines for managing patients with primary ER+ HER2- breast cancer deferred from surgery due to the COVID-19 pandemic. NPJ Breast Cancer. 2020;6:21.

25. Fontein DB, Charehbili A, Nortier JW, et al. Efficacy of six month neoadjuvant endocrine therapy in postmenopausal, hormone receptor-positive breast cancer patients--a phase II trial. Eur J Cancer. 2014;50(13):2190-2200.

26. Rusz O, Voros A, Varga Z, et al. One-Year Neoadjuvant Endocrine Therapy in Breast Cancer. Pathol Oncol Res. 2015;21(4):977-984.

27. Krainick-Strobel UE, Lichtenegger W, Wallwiener D, et al. Neoadjuvant letrozole in postmenopausal estrogen and/or progesterone receptor positive breast cancer: a phase IIb/III trial to investigate optimal duration of preoperative endocrine therapy. BMC Cancer. 2008;8:62.

28. Francis A, Thomas J, Fallowfield L, et al. Addressing overtreatment of screen detected DCIS; the LORIS trial. Eur J Cancer. 2015;51(16):2296-2303.

29. Elshof LE, Tryfonidis K, Slaets L, et al. Feasibility of a prospective, randomised, open-label, international multicentre, phase III, non-inferiority trial to assess the safety of active surveillance for low risk ductal carcinoma in situ - The LORD study. Eur J Cancer. 2015;51(12):1497-1510.

30. Hwang ES, Hyslop T, Lynch T, et al. The COMET (Comparison of Operative versus Monitoring and Endocrine Therapy) trial: a phase III randomised controlled clinical trial for low-risk ductal carcinoma in situ (DCIS). BMJ Open. 2019;9(3):e026797.

31. Ryser MD, Weaver DL, Zhao F, et al. Cancer Outcomes in DCIS Patients Without Locoregional Treatment. J Natl Cancer Inst. 2019;111(9):952-960.

32. Curigliano G CM, Poortmans P, Gentilini O, Pravettoni G, Mazzocco K et al. . Recommendations for triage, prioritization and treatment of breast cancer patients during the Covid-19 pandemic. . The Breast 2020.

33. The COVID-19 Pandemic Breast Cancer Consortium. https://www.facs.org/-/media/files/quality-programs/napbc/asbrs_napbc_coc_nccn_acr_bc_covid_consortium_recommendations.ashx. Published 2020. Accessed 17/04/2020.

34. Bashshur R, Doarn CR, Frenk JM, Kvedar JC, Woolliscroft JO. Telemedicine and the COVID-19 Pandemic, Lessons for the Future. Telemed J E Health. 2020.

See http://www.TheOncologist.com for supplemental material available online.

Table 1. Virtual meeting results

	Phase	Lockdown*	Screening	Management at admission	Surgical prioritization	Alternatives	Reconstruction	Out-patients
China	/	23rd January	Stopped	Provenience Clinical history Temperature screening CT scan; nucleic acid detection from samples of throat swabs One patient one single room Mask to all patients	Surgical procedures that cannot be postponed: 1Patients finishing NAC 2 Cancer progressing during NAC 3 DCIS 4 Malignant tumor such as sarcoma or malignant phyllodes tumor	NAC according to standard criteria	Simplify reconstruction method (only implant-based reconstruction, or tissue expander if possible PMRT) to reduce risks of complications and shorten time of exposure decrease robot /free flap reconstruction	WeChat group/email Used during emergency Self-protection and social distancing advised
Italy (Lombardy)	II	15th March	Stopped	Clinical history temperature screening, blood check, SpO_2, X-Ray Eventual swab or low-dose CT in selected cases. Suspicious cases were postponed (1-2weeks). Visits mainly for preop / postop patients. "Hub and spokes" hospital model	**In 2-4 weeks:** Cancer progressing during NAC; Premenopausal patients with aggressive disease not candidate to NAC; Local-regional recurrence within 48 months, pregnant patients; patients with complications **In 4 and 8 weeks** Grade 2 tumors, premenopausal patients with T<3 cm, N0 cancer not candidate to NAC, post-neoadjuvant patients **> 8 weeks:** grade 1 tumors, DCIS, benign disease	NAC according to standard criteria **Endocrine therapy** as a bridge to surgery in ER+ tumors out of priority criteria. Outside standards MDT decision is needed	Only immediate implant-based reconstruction after mastectomy is allowed.	Post-surgery and "urgent" visits (3-10 days) Email/phone calls Telemedicine service
Iran	II	20th March	Stopped	Any travel or close contact. Clinical history Temperature screening, SpO2 Chest CT and COVID test only after consultation and for suspicious cases	**Priority A/B** **A**:as soon as possible: Drainage of breast abscess / hematoma / Ischemic flap **B1**: start treatment before the pandemic is over:	**NAC** according to standards and for chemo/anti Her" agents sensitive irrespective of stage (except for TNBC stage1) **Endocrine therapy for:** - ER+/Her2- (Luminal-A-like	No reconstruction	Post-surgery and follow-up done remotely

(continued)

Table 1. (continued)

	Phase	Lockdown*	Screening	Management at admission	Surgical prioritization	Alternatives	Reconstruction	Out-patients
				(if positive: admission denied) All procedures done as day cases	Refractory or progressive case under Neoadjuvant therapy/ Malignant Phyllodes tumor/ Cancer in first trimester of pregnancy/ Diffuse or big comedo type DCIS **B2**:if resources are enough: Post Neoadjuvant cases/ T1 N0/T2 N1 Luminal cases/ Stage 1 TripleNegative/ Discordance biopsy likely to be Malignant/ Recurrent disease/ DCIS ER negative	cases), reevaluate after 3 months ER+ BC finishing NAC with partial/ complete clinical, consider converting to endocrine therapy in order to delay surgery versus surgery for 4-8 weeks		
Spain (private)	I	29th March	Stopped	Clinical history Temperature screening Contacts If suspicious admission denied and referred to swab test. Negative PCR required to receive surgery Same day discharge Visits mainly for preop / postop patients.	Surgical procedures that cannot be postponed (Patients finishing pre-op systemic treatment)	**NAC** according to standard criteria **Endocrine therapy** according to standard criteria and for premenopausal patients ESBC HR +/HER2 neg	Implant-based reconstruction It is offered if low risk of complications. (Low BMI, no smokers, no comorbidities, <60 years).	Limitations at the waiting room No follow-up. Telematic consultation whenever possible
Spain			(Academic)	III	29th March	Stopped	Clinical history Temperature screening contacts history Negative PCR required to receive surgery Same day discharge	Surgical procedures that cannot be postponed (Patients finishing pre-op systemic treatment)

(continued)

Table 1. (continued)

	Phase	Lockdown*	Screening	Management at admission	Surgical prioritization	Alternatives	Reconstruction	Out-patients
							Visits mainly for preop / postop patients.	
NAC according to standard criteria **Endocrine therapy** according to standard criteria and for			premenopausal patients ESBC HR +/HER2 negative	Implant-based reconstruction	Limitations at the waiting room No follow up. Telematic consultation whenever possible			
Uk(England)	II	23rd March	Stopped	Clinical history Physical examination PCR test if available to every patient Recent CT chest (last 24h) or failing that CXR. Clip all cancers when biopsy performed. Aim for day case surgery. Do minimum. Minimum staff in theatre and appropriate PPE for all staff All patients are intubated and extubated in theatre	Surgical priority given to ER negative patients first. Then HER2+ patients. Post NAC. High grade DCIS (ER+ started on HT, ER- candidate for surgery) If highly suspicious COVID 19 infection or positive test, postpone surgery 2/52 then re – evaluate. Incise tumor and mark it – To reduce specimen manipulation by pathologists (Protect pathologists). All specimens are fixed in formalin.	**NAC** only for inoperable patients **Endocrine therapy** according to standard criteria and for ER+ DCIS (all core biopsies demonstrating DCIS should be tested for hormone receptor status) perform genomic testing on the biopsy specimen for invasive breast cancer , and consider endocrine therapy; ER+/HER2- BC post-NAC: consider converting to endocrine therapy in order to delay surgery. - ER+/HER2+ BC post-NAC: consider converting to NET + anti-HER2 therapy in order to delay surgery	No reconstruction	Triage all referrals. Telephone consultation. Face- to –Face clinic ; 5-6 patients per clinic -30 minutes slot each. >=70 year old patients or patients with significant co-morbidities; no clinic visit. Only phone consultation. Start empirical HT if suspicious.
UK(Scotland)	I	23rd March	Stopped				- No reconstruction	

(continued)

Table 1. (continued)

	Phase	Lockdown*	Screening	Management at admission	Surgical prioritization	Alternatives	Reconstruction	Out-patients
				COVID test only for symptomatic patients (Clinical History Highly suspicious need PCR testing If safe, perform procedures as day surgery)	Surgical priority given to ER negative patients first. Then HER2+ patients. Post NACT. High grade DCIS (ER + started on HT, ER - candidate for surgery) If highly suspicious COVID 19 infection or positive test, postpone surgery 2/52 then re – evaluate. Incise tumor and mark it – To reduce specimen manipulation by pathologists (Protect pathologists). All specimens are fixed in formalin.	**NAC** according to standard criteria **Endocrine therapy:** - ER+ DCIS (all core biopsies demonstrating DCIS should be tested for hormone receptor status) - ER+/HER2- BC (perform genomic testing on the biopsy specimen, and consider endocrine therapy or NAC if appropriate) - ER+/HER2- BC post-NAC: consider converting to endocrine therapy in order to delay surgery. - ER+/HER2+ BC post-NAC: consider converting to NET + anti-HER2 therapy in order to delay surgery.		- All urgent referrals are accepted. Routine referrals postponed/cancelled.
USA (NYC)	II	22nd March	Stopped	Telephone Triage Clinical history Temperature screening Blood check SpO2 COVID test	Life-threatening conditions: breast abscess in a septic patient, expanding hematoma Urgent cases: ischemic autologous tissue flap/mastectomy flap, post-NAC patients, progression under NAC BCS is preferred provided that radiation oncology services are available and the	**NAC for** -TNBC/Her2+ (≥ T2 or N1) Some ER+/HER2- -Inflammatory/ locally advanced BC **Endocrine therapy:** - ER+ DCIS (all core biopsies demonstrating DCIS should be tested for hormone receptor status) - ER+/HER2- BC (perform genomic testing on the biopsy specimen, and consider	Limited to tissue expander or definitive implant placement. Autologous reconstruction should be deferred	The majority of encounters are conducted remotely via telemedicine. If need for in-person evaluation special measures to reduce the risk of infection are put in place.

(continued)

Table 1. (continued)

	Phase	Lockdown*	Screening	Management at admission	Surgical prioritization	Alternatives	Reconstruction	Out-patients
					risk of multiple visits or deferred radiation is acceptable. If no ventilator available or high risk of exposure, BCS can be performed under local anesthesia via sedation.	endocrine therapy or NAC if appropriate) - ER+/HER2- BC post-NAC: consider converting to endocrine therapy in order to delay surgery. - ER+/HER2+ BC post-NAC: consider converting to NET + anti-HER2 therapy in order to delay surgery.		
Sweden	I		Decision on a regional level; decreased participation	COVID test only for symptomatic patients If medically safe, perform procedures as day surgery.	Priority as follows: Patients that have completed/ discontinued primary chemotherapy > TNBC, HER2+ > LumB > LumA, DCIS grade 3 with larger size.	**NAC** according to standard criteria **Endocrine therapy:** - > 70 yrs, LumA or B N0/1 - 60-70 yrs LumA N0	- Perform breast reconstruction in exceptional cases; choose the simplest alternative	-only absolutely necessary referrals -Calls, video calls when appropriate
Denmark	I	12th March	Unchanged	COVID test only for symptomatic patients	BIRADS 4 and 5 lesions treated as always BIRADS 3 treated on MDT decision BIRADS 1-2 postponed	**NAC** according to standard criteria Patients informed on potential risks of chemotherapy during the COVID 19 pandemic	- As usual, some limitations for the DIEP flap	Normal consultations (only distancing) for BIRAD4-5 and some BIRADS3
Switzerland (Italian speaking part)	I	16th March	Stopped	COVID test for all symptomatic patients within 48 hours before surgery	Standard indications to surgery	**NAC, including immune- and endocrine therapy** according to standard criteria	Standard indications for breast reconstruction if beneficial for patient, including autologous reconstruction	Consultations limited to only not deferrable ones Most consultations via telephone, video calls or e-mail
Portugal	I	18th March	Stopped	Clinical History Physical examination Temperature screening Chest X-Ray WBC	Patients completing NAC Only level I oncoplastic breast conserving surgery	**NAC** according to standard criteria	No reconstruction	Urgent referrals only Face masks for all patients and social distance in waiting room

(continued)

Table 1. (continued)

Phase	Lockdown*	Screening	Management at admission	Surgical prioritization	Alternatives	Reconstruction	Out-patients
			COVID test for all symptomatic patients				

NAC neoadjuvant chemotherapy; DCIS ductal carcinoma in situ; PMRT post mastectomy radiotherapy; ER estrogen receptors; MDT multidisciplinary team; ESBC early stage breast cancer; BMI body mass index; PCR polymerase chain reaction; HT Hormonal therapy; BC breast cancer; TNBC triple negative breast cancer; WBC white blood cells; DIEP deep inferior epigastric perforator; LumA Luminal A; LumB Luminal B; PPE Personal Protection Equipment

Lockdown dates as reported on https://en.wikipedia.org/wiki/Curfews_and_lockdowns_related_to_the_2019%E2%80%9320_coronavirus_pandemic (except for IRAN)

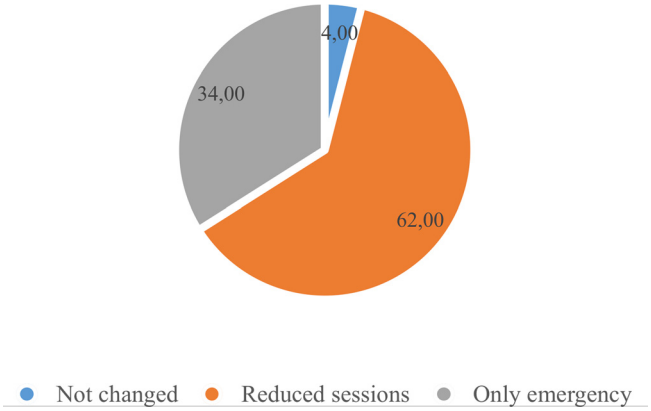

Figure 1. Operating room schedules distribution

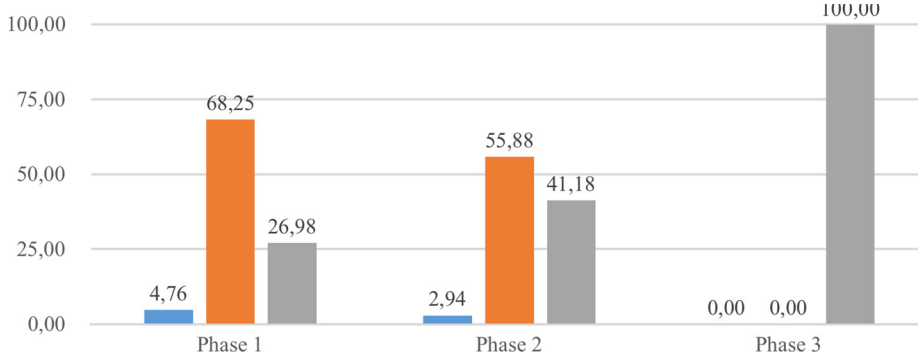

Figure 2. Changes in the OR schedule according to the ACS phase

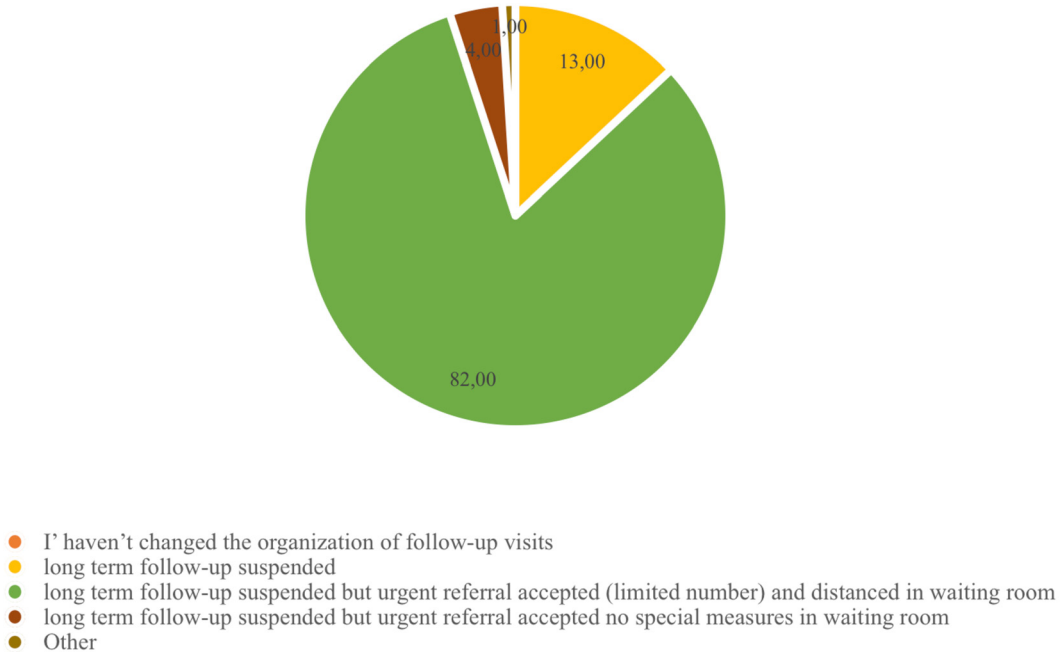

Figure 3. Organization of consultations/ long term follow-up visits

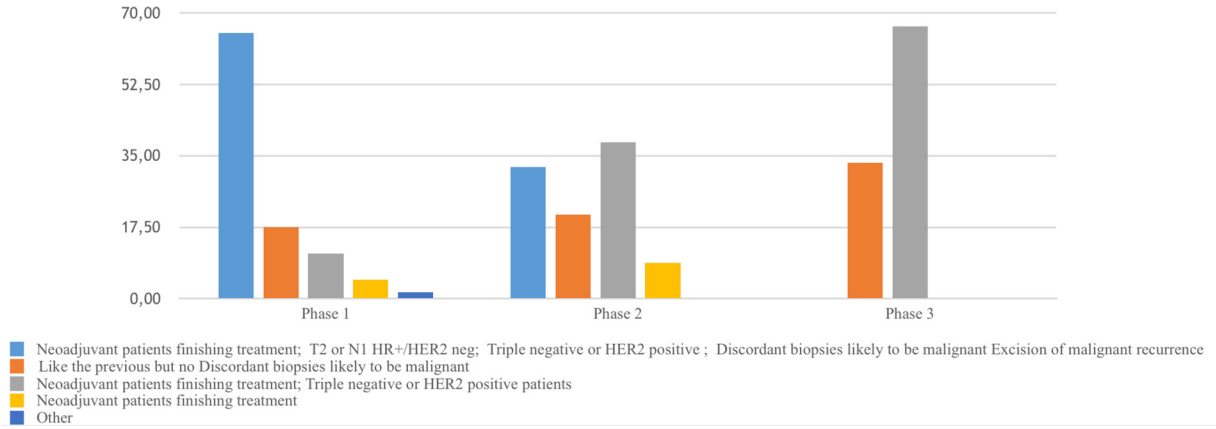

Figure 4. Changes in the surgical priorities according to the ACS phase

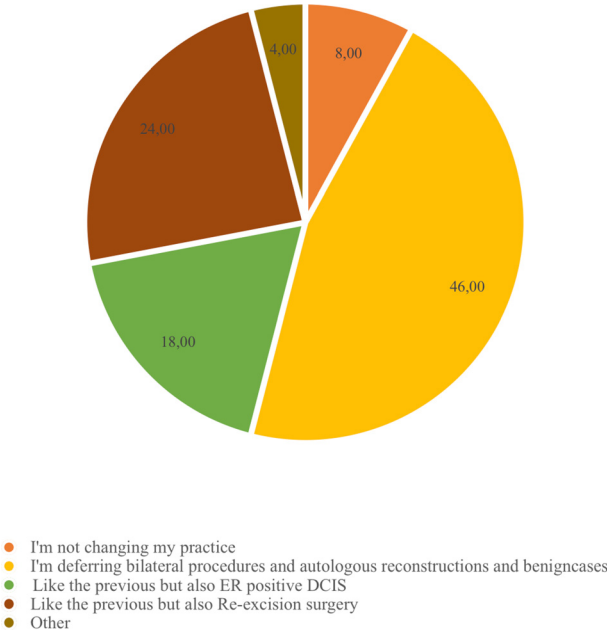

Figure 5. Cases that can be deferred distribution

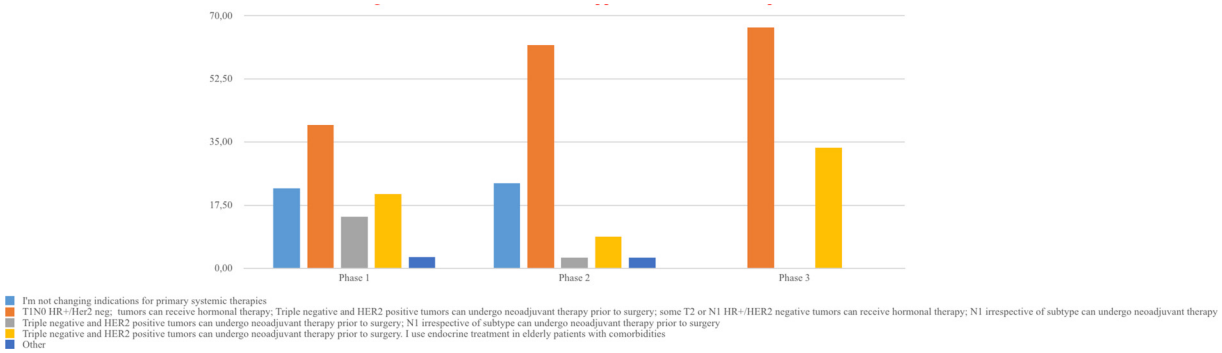

Figure 6. Changes in the alternative treatment approach according to the ACS phase